Remarks:

Claims

By the present amendment, claims 27, 29, 32, 34-35, 38 and 43 have been amended to more particularly and distinctly describe the invention; claims 56-59 have been added to more particularly claim certain embodiments of the invention; and claims 52-55 have been cancelled without prejudice. Claims 27, 29, 32, 34-35, 38, 43-44, 46, and 56-59 are pending.

It is believed that the total number of total claims and of independent claims remains less than the amount for which fees were previously paid. Notwithstanding, Applicant hereby authorizes the Commissioner to charge for any additional claim fees that may be due to Account No. 50-0258.

Support for recombinant polypeptide found in the amended and new claims can be found, for example, at page 1, lines 5-7; page 4, lines 1-8; page 7, lines 7-14; page 8, lines 1-7; and page 9, lines 1-5.

Reconsideration of the rejections is respectfully requested.

Claim Rejections - 35 U.S.C. §112, First Paragraph -Written Description

Claims 27, 29, 32, 34, 38, 43-44, 46, and 50-55 stand rejected under 35 U.S.C. §112, first paragraph based on an assertion the claims contained subject matter that was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventor, at the time, the application was filed, had possession of the claimed invention. In particular, the Examiner asserted that the specification does not teach fragments, and fusion proteins and immunogenic compositions comprising the fragments. The Examiner further alleges that the specification fails to teach the structure or relevant identifying characteristics of fragments of SEQ ID NO:2, sufficient to allow one of skill in the art to determine that the inventor had possession of the invention as claimed.

Applicant respectfully disagrees. Applicant submits that the Notice, entitled, "*Guidelines for Examination of Patent Applications under the 35 U.S.C. 112, ¶1. Written Description" Requirement* at p. 1104, vol 66, no. 4 (January 5, 2001) addresses the written description provision as follows (emphasis added):

> An applicant shows possession of the claimed invention with all its

> limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing characteristics sufficient to show that the applicant was in possession of the claimed invention.

Applicant notes that the specification discloses an immunogenic fragment of a BASB109 polypeptide, that is a contiguous portion of the BASB109 polypeptide which has the same or substantially the same immunogenic activity as the polypeptide comprising the amino acid sequence of SEQ ID NO:2 at, for example, page 5, lines 20-24. In addition, the specification further describes preferred fragments including an isolated polypeptide comprising amino acid sequence having at least 15 contiguous amino acids of SEQ ID NO:2 at, for example, page 6, lines 21-25. Applicant submits that these recitations of the immunogenic fragments, coupled with the disclosed amino acid sequence of SEQ ID NO:2 represent possession of the invention by showing that the invention was "ready for patenting" by the disclosure of structural chemical formulas that show the invention was complete. Reconsideration of the Written Description Requirement rejection under 35 U.S.C. 112, ¶1 is therefore respectfully requested.

Claim Rejections - 35 U.S.C. §112, First Paragraph - Enablement

Claims 27, 29, 32, 34, 38, 43-44, 46 and 50-55 stand rejected under 35 U.S.C. §112, first paragraph based on an assertion that the specification, while being enabling for a polypeptide consisting of the sequence of the amino acid SEQ ID NO: 2 and a fusion protein comprising the amino acid sequence SEQ ID NO:2, does not reasonably provide enablement for an isolated polypeptide that comprises a fragment of at least 15 or 20 amino acids, fusion protein or immunogenic composition comprising said fragments.

The rejection includes a general discussion of the unpredictability of protein chemistry, and on the consequences of a single change in an amino acid residue on the biological activity of a protein. The specification, according to the Examiner, has not taught which residues of SEQ ID NO:2 can still be varied and still achieve a polypeptide that is functional as a diagnostic using

immunological means of recognition. The rejection concludes by asserting that the skilled artisan would be forced into undue experimentation to practice the invention as claimed.

Applicant respectfully disagrees. Whether the scope of enablement is sufficient is often decided in light of the following factors: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors are illustrative, not mandatory. Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991). A review of these factors as applied to the present claims, supports Applicant's assertion that the claims are enabled, as outlined in subsections (A) through (G) below.

(A) *Quantity Of Experimentation*

In Reece (Reece et al., 151 J. IMMUNOL. 6175 (1993), attached as Exhibit A)[1], in excess of one thousand (1,304) overlapping 12 residue peptide fragments were synthesized by the multipin method to map T-cell epitopes of tetanus toxin. Pools of 20 peptides each were used to simplify the mapping assays. Thus, it was practical to synthesize a large number of peptides, and the initial screen needed only to assay sixty to seventy pools. Pools that generated strong responses were deconvoluted by assaying the members of the pool. That such experimentation using a multipin method to screen for antigens is ordinary in this art is illustrated in CURRENT PROTOCOLS IN IMMUNOLOGY 9.7.1 (1997) (attached as Exhibit B) and Reece et al., 172 J. IMMUNOL. 241 (1994) (attached as Exhibit C). That such sequence-scanning techniques are ordinary in the art with respect to antibody-mediated antigenicity (as opposed to cellular immunity as in Reece) is illustrated in Geysen et al., 81 PROC. NATL. ACAD. SCI. USA 3998 (1984) (attached as Exhibit D).

---

[1] The literature cited in this response provides evidence of the state of the art – and is not submitted under 37 CFR §1.56.

Note that in Geysen, antisera to the whole antigen polypeptide was tested for specificity with an extensive scan of specific peptide sequences. This approach is quite useful to the present invention, where the full-length recombinant BASB109 polypeptide that Applicant has isolated can readily be used within the state of the art to produce polyclonal antibodies. These polyclonal antibodies can then be used to screen for promising smaller polypeptide antigens.

(B) *Amount Of Direction Or Guidance Presented*

Guidance can be found in the specification at, for example, page 6, lines 10-19:

> Preferred fragments include, for example, truncation polypeptides having a portion of an amino acid sequence of SEQ ID NO:2 or 4 or of variants thereof, such as a continuous series of residues that includes an amino- and/or carboxyl-terminal amino acid sequence. Degradation forms of the polypeptides of the invention produced by or in a host cell, are also preferred. Further preferred are fragments characterized by structural or functional attributes such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions.

That the sequence-based inferences described here are ordinary in the art, and of known value in selecting positive candidates is illustrated by CURRENT PROTOCOLS IN IMMUNOLOGY 9.3.1 (1991) (attached as Exhibit E).

(C) *Presence Or Absence Of Working Examples*

The specification illustrates the isolation of a full length recombinant BASB109 protein (Example 3). While the specification does not specifically provide a detailed working example of the isolation of immunogenic fragments of SEQ ID NO: 2, Applicant submits that a skilled artisan, given the teachings of the specification and recombinant techniques well known in the art, could readily prepare recombinant polypeptides comprising the claimed fragments of SEQ ID NO:2. Recombinant polypeptides comprising the fragments could then be used to produce protein-recognizing anti-sera using well-known immunological techniques. The anti-sera's potential for detecting the presence of SEQ ID NO:2 can then be determined. In addition, the

ease with which the polypeptides are screened, and the availability of robotic automation tools at the time the application was filed, counterbalance this element of the analysis.

(D) *Nature Of The Invention; Predictability Or Unpredictability Of The Art*

The art is no more unpredictable than the chemical arts in general. Thus, the reasonable scope of the claims should be comparable to that which can be achieved with other structure-focused claims in the chemical arts. Moreover, the ease with which the polypeptides are screened, and the availability of robotic automation tools at the time the application was filed, counterbalance this element of the analysis.

That an unpredictable art nonetheless allows for reasonable inferences of claim scope is illustrated by the following text from the case law:

> Appellants have apparently not disclosed *every* catalyst which will work; they have apparently not disclosed *every* catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with *every* species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used in "forming hydroperoxides."

Application of Angstad, 537 F.2d 498, 502-3, 190 USPQ 214, 218 (CCPA1976) (emphasis in the original).

(E) *State Of The Prior Art*

The highly advanced state of this art is illustrated by the above cited 1984 article by Geysen. The other articles discussed above clearly show that sequence scanning for antigenicity is a highly developed art.

(F) *Relative Skill Of Those In The Art*

In Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999), the Federal Circuit approved a trial court determination in a comparable art that a person of ordinary skill would be a junior faculty member with one or two years of relevant experience or a postdoctoral student with several years of experience. Applicants respectfully submit that this level of skill is an appropriate measure of skill in the present context.

(G) *Breadth Of The Claims*

The instant claims focus on a limited universe of claimed core elements. The world of the instant claims is miniscule compared to the monoclonal antibody world approved for claiming in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors thus weigh in favor of the allowability of the present claims. Accordingly, reconsideration of the rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

Claim Rejection - 35 U.S.C. §102(b) - Helminen et al.

Claims 27, 29, 32, 34, 38, 43-44, 46, and 50-55 stand rejected under 35 U.S.C. §102(b) based on an assertion that the claims are anticipated by Helminen et al. (J. Infec. Dis., 170, 1994, pp 867-872). In particular the Examiner asserted:

> Helminen et al 1994 disclose an isolated polypeptide, outer membrane protein i.e., OMP from whole cell lysate in a buffer from M.catarrhalis. The antigen to which an immune response has to be elicited is in general in a hydrophilic phase (i.e., buffer). Mice were immunized with whole cell lysate antigens to mice (page 867, right column through page 868, left column, first paragraph) to produce antibodies. Therefore, it reads on immunogenic composition. It is inherent that the whole cell lysates contain more than one protein and read on fusion proteins as well. Applicant's use of the open-ended term "comprising" in the claim 27 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed isolated polypeptide, OMP from M.catarrhalis. Whole cell lysate from M.catarrhalis appears to contain an isolated

> polypeptide SEQ ID NO:2. Characteristics such as SEQ ID NO: 2 are considered as inherent properties of the polypeptide that was present in the lysate disclosed by the prior art. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S. P.Q. 448 (PTO d. App. 1948). Since the Office does not have the facilities for examining and comparing applicants' claimed product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Without conceding the correctness of the rejection, Applicant has amended the claims to more particularly and distinctly claim the subject matter of his invention. It is submitted that the amended claims recite an isolated, recombinant polypeptide. The claimed isolate is not disclosed or suggested by the OMP preparations described in Helminen et al.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) over Helminen et al. is respectfully requested.

Claim Rejection - 35 U.S.C. §102(b)- Hoehn et al.

Claims 27, 29, 32, 34, 43, 46, 40 and 52-55 stand rejected under 35 U.S.C. §102(b) based on an assertion that the claims are anticipated by Hoehn et al. (Infection and Immunity, 1992, 60, 4695-4703 and Accession No. Q02219). The Examiner noted a happenstance overlap of the amino acid sequence of the disclosed protein with amino acids 178-211 of SEQ ID NO:2 of the instant application.

Without conceding the correctness of the rejection, Applicant has amended claim 27 and 34 so that to more particularly and distinctly define his invention. Applicant submits that by the amendments, claims 27 and 34 recite fragments that are not disclosed by the amino acid sequence of the protein of Hoehn et al.. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Amendments to the Specification:

In view of the number of amendments to the specification suggested by the Examiner, Applicants have elected to submit a substitute specification pursuant to 37 CFR 1.125. A

markup specification that highlights the changes in the specification is also included. Entry of the amendments to the specification is respectfully requested.

The substitute specification includes a section entitled "Brief Description of the Drawings." Support for the descriptions of the drawings can be found in the drawings as originally filed, and no new matter is added. The drawing descriptions are consistent with the proposed amemdments to the drawing figures described below and in the replacement sheets.

In addition, the recitation "What is claimed is:" has been added to the claims section to secure consistency with MPEP 608.01(a). An abstract on a separate sheet is also provided.

Amendments to the Drawing Figures:

Replacement of the figures of record in the application with the concurrently filed replacement figures is respectfully requested. The figures have been amended to comply with 37 CFR 1.84. No new matter has been added.

Figure 1 has been relabeled as Figures 1A-1H, and the title text has been removed. Figure 2 has been relabeled as Figures 2A-2D, and the title text has been removed. The title text from Figure 3 has been removed, the description of which has been inserted in the Brief Description of the Drawings (see above). No new matter has been added.

FEE DEFICIENCY

☒ If an extension of time is deemed required for consideration of this paper, please consider this paper to comprise a petition for such an extension of time; The Commissioner is hereby authorized to charge the fee for any such extension to Deposit Account No. 50-0258.

and/or

☒ If any additional fee is required for consideration of this paper, please charge Account No. 50-0258.

Closing Remarks

Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration in view of this response and allowance of the pending claims are earnestly solicited.

Respectfully submitted,

E.C. Meade

Eric A. Meade
Registration No. 42,876
for
Allen Bloom
Registration No. 29,135
Attorney for Applicant

DECHERT LLP
A Pennsylvania Limited Liability Partnership
Princeton Pike Corporate Center
PO Box 5218
Princeton, New Jersey 08543-5218
Phone: (609) 620-3248
Fax: (609) 620-3259